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Original Research

A novel predictor behind conventional risk factors of new-onset atrial fibrillation after off-pump coronary artery bypass graft surgery: The triglyceride-glucose index

TyG index: A new predictor for POAF in CABG surgery

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Abstract

Aim: Atrial fibrillation (AF), which frequently occurs after coronary artery bypass graft surgery (CABG), raises the risk of adverse events such as stroke and heart failure. Insulin resistance (IR) is a major risk factor for developing postoperative AF (POAF), and the triglyceride-glucose (TyG) index offers a more precise and reliable assessment of IR compared to the homeostasis model. This study investigated the correlation between preoperative TyG index levels and POAF in patients undergoing off-pump CABG.

Material and Methods: Four hundred sixteen patients undergoing isolated off-pump CABG were included in the study. The preoperative TyG index and the presence of POAF were evaluated in all patients. Significant variables (P<0.05) from univariate analysis were included in multivariate logistic regression to identify potential POAF risk factors. The TyG index's predictive efficacy for POAF was assessed in two models: one with conventional risk factors and the other adding the TyG index.

Results: POAF was detected in 106 patients (25.5%), with significantly higher TyG index levels observed in POAF patients compared to those without POAF [9.8 (8.0-11.7) vs. 9.0 (7.7-11.1), P<0.001]. The TyG index was found to be an independent predictor of POAF (P<0.001) with moderate predictive power (AUC=0.767). Adding the TyG index to the model, which included age and left atrial diameter, significantly improved its predictive capacity for POAF (P=0.038).

Discussion: In our retrospective study, we identified the TyG index as an independent predictor of POAF in patients undergoing off-pump CABG.

Keywords

Triglyceride-Glucose Index, Atrial Fibrillation, Off-Pump, Coronary Artery Bypass Grafting, Insulin Resistance

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Introduction

Atrial fibrillation (AF) is the prevailing arrhythmia that manifests after coronary artery bypass graft surgery (CABG), and is present in approximately 33% of cases, typically within the first few days after the procedure. Noteworthy risk factors, including advanced age, impaired ventricular function, hypertension, and left atrial dilatation, are closely linked to the development of postoperative AF (POAF) [1, 2]. However, it may be crucial to identify high-risk patients for POAF before CABG, as it enables preoperative preventive measures and evaluation of modifiable risk factors.

Insulin resistance is associated with inflammation and oxidative stress, which have been identified as contributing factors in the remodeling of the left atrium. Studies have shown IR is a recognized risk factor for developing POAF following CABG [3, 4]. However, there remains a gap in a practical and accessible clinical tool that can predict the AF after CABG and provide insights into IR.

The hyperglycemic-hyperinsulinemic clamp test is the reference method for evaluating IR in clinical settings. Although this test provides a comprehensive examination of IR by accurately measuring the insulin sensitivity of peripheral tissues, given the difficulties in conducting the hyperglycemic-hyperinsulinemic clamp test, the homeostasis model is often employed as a convenient option for evaluating IR in clinical practice [5]. However, this test has limitations because of the need to measure fasting blood insulin [5], which is not routinely conducted. In the context of evaluating IR, the triglyceride-glucose (TyG) index, which can be conveniently emanated from triglyceride and glucose measurements, may offer a more accurate and reliable assessment compared to the traditional homeostasis model [6, 7]. The primary focus of this study was to investigate the association between preoperative TyG index levels and the development of POAF in patients undergoing off-pump CABG.

Material and Methods

Study Population

This retrospective cross-sectional study enrolled 515 patients who received off-pump CABG at the Department of Cardiovascular Surgery, from January 2015 to November 2022 and had no previous history of AF. The inclusion criteria included being 18 years or older, undergoing their first off-pump CABG procedure after acute coronary syndrome or elective coronary angiography, and having normal sinus rhythm. The decision to focus specifically on the off-pump CABG technique was made to minimize confounding factors related to different surgical approaches based on the higher prevalence of its use in our clinic. Exclusion criteria included a history of high-degree heart block or permanent pacemaker placement, cardiogenic shock, left atrial diameter ≥55mm, severe valve pathologies (stenosis or regurgitation), previous paroxysmal AF attacks, prior amiodarone treatment, autoimmune diseases, malignancy, pregnancy, hyperthyroidism, chronic kidney failure patients receiving hemodialysis or peritoneal dialysis, advanced stage liver disease, and the need for additional procedures such as valvular surgery or left ventricular aneurysmectomy. As a primary outcome, we evaluated the occurrence of POAF during the hospitalization period.

Surgical technique and procedural strategies

For all patients, the surgical technique chosen was off-pump CABG. All patients underwent off-pump CABG surgery through midline sternotomy using standard surgical techniques. Saphenous vein grafts were harvested for conduit, and internal mammary artery grafts were utilized in most patients (93.5%). Potassium levels were closely monitored and maintained within the 4.0-4.5 mEq/L range. As part of our clinic's standard postoperative protocol, all patients received oral metoprolol succinate tablets ranging from 25 to 200 mg to maintain heart rates below 80 bpm.

Laboratory assessments

The demographic and clinical characteristics and the preoperative triglyceride and glucose values were meticulously obtained by thoroughly reviewing the patients' medical charts. Before the operation morning, all patients underwent standard laboratory tests following a minimum 8-hour period of fasting. Fasting serum triglyceride and glucose levels were measured using an automated analyzer, specifically the Roche Cobas 8000 (Roche Diagnostics, Mannheim, Germany), and the TyG index calculated as ln [fasting TG (mg/dL) × fasting plasma glucose (mg/dL)/2].

Cardiac rhythm evaluation

Cardiac rhythm assessment was performed using bedside monitors and twelve-lead electrocardiograms (ECGs) immediately after the surgery and daily until patients were discharged. All ECGs recordings obtained from patient files and clinical observation records were used. Postoperative atrial fibrillation was described as AF lasting at least 5 minutes or requiring cardioversion with electrical or antiarrhythmic drugs.

Echocardiographic measurements

All patients underwent transthoracic echocardiography using a Philips EPIQ 7C ultrasound machine with a S5-1 transthoracic probe. The echocardiographic evaluation included measurements of left atrial anteroposterior diameter, ejection fraction, and assessment of valve pathologies.

Statistical Analysis

The Kolmogorov-Smirnov test evaluated the distribution of the data's normality, and variables were shown as percentages (%), means with standard deviations (±), and medians with minimum and maximum values (min-max). Group comparisons of continuous variables were conducted using independent sample t-tests or Mann-Whitney U tests, as appropriate. Categorical variables were evaluated under the chi-square test. The threshold for the TyG index in predicting POAF was determined using Receiver Operating Characteristic (ROC) analysis. To identify potential risk factors for POAF, significant variables from the univariate analysis (P-value <0.05) were included in the multivariate logistic regression models. The backward method was employed for all regression analyses. The predictive performance of the TyG index for POAF was compared between two models: one included conventional risk factors reported in the literature, while the other conventional risk factors plus the TyG index. A value of P<0.05 was used to determine statistical significance, and IBM SPSS Statistics version 26 software (IBM Corp., Armonk, NY) was used for all statistical analyses.

Ethical Approval

This study was approved by the Ethics Committee of Karabuk University (Date: 2022-12-19, No: 2022/1171).

Results

Of the 515 patients at baseline, 56 were excluded because of missing pre-CABG triglyceride values, 23 did not meet the diagnostic criteria for AF episodes, and 20 did not meet the other criteria, leaving 416 patients in the analysis (Figure 1). The study patients' demographic characteristics, echocardiographic findings, and laboratory results are presented in Table 1. The study included predominantly male participants (78.1%) with a median age of 64 years (40-86). Following the surgery, POAF was identified in 106 patients (25.5%). The POAF group had higher TyG index figures in comparison to those without POAF [9.8 (8.0-11.7) vs. 9.0 (7.7-11.1), P<0.001].

Patients with POAF had a higher body mass index [29.4 (19.7-51.0) vs. 27.8 (17.0-44.1) kg/m2, P=0.010], and a higher prevalence of hyperlipidemia (P=0.029), hypertension (P<0.001), and diabetes (P=0.002) compared to those without POAF.

Patients with POAF had greater left atrial anteroposterior diameter (41.6 ± 4.2 vs. 37.4 ± 3.5 mm, P<0.001) and lowered

Table 2. Logistic analysis for predictors of postoperative atrial fibrillation

Characteristics	OR	95% CI	P Value
Univariate logistic regression analysis			
Age	1.087	1.056–1.119	<0.001
Male	1.407	0.843–2.350	0.191
Body mass index	1.078	1.027–1.131	0.002
Hypertension	0.261	0.140–0.489	<0.001
Diabetes mellitus	0.482	0.304–0.763	0.002
Hyperlipidemia	0.601	0.379–0.951	0.030
Left atrial diameter	1.344	1.250–1.446	<0.001
Left ventricular end-diastolic diameter	1.059	1.005–1.115	0.031
Left ventricular ejection fraction	0.959	0.937–0.982	0.001
Mild or moderate mitral regurgitation	0.030	0.007–0.126	0.060
Mechanical ventilation time	1.130	1.056–1.209	<0.001
TyG index	5.402	3.557–8.202	<0.001
Multivariate logistic regression analysis			
Age	1.047	1.006–1.090	0.025
Left atrial diameter	1.373	1.243–1.518	<0.001
TyG index	6.824	3.511–13.264	<0.001

Abbreviations: TyG; Triglyceride glucose index.

Table 1. Clinical characteristics of the study population

Variables	Whole cohort	No POAF (n=416)	POAF (n=310)	P-value (n=106)
Age (years)	64 (40–86)	62 (41–86)	70 (40–82)	<0.001
Male, n(%)	325 (78.1)	245 (79.0)	80 (75.5)	0.191
Hypertension, n(%)	295 (70.9)	202 (65.2)	93 (87.7)	<0.001
Diabetes mellitus, n(%)	220 (52.9)	150 (48.4)	70 (66)	0.002
Hyperlipemia, n(%)	237 (57.0)	167 (53.9)	70 (66)	0.029
Body mass index (kg/m2)	28.0 (17.0–51.0)	27.8 (17.0–44.1)	29.4 (19.7–51.0)	0.010
Timing of CABG				
Within the first week following ACS, n(%)	78 (18.8%)	36 (11.6%)	42 (39.7%)	<0.001
1-4 Weeks Following ACS, n(%)	246 (59.1%)	211 (68.1%)	35 (33.0%)	0.001
After Elective Coronary Angiography, n(%)	92 (22.1%)	63 (20.3%)	29 (27.3%)	0.072
Laboratory factors				
Creatinine (mg/dL)	1.0 ± 0.4	1.0 ± 0.3	1.0 ± 0.5	0.953
eGFR (mL/min/1.73 m2)	79.9 ± 18.2	79.9 ± 17.7	79.6 ± 19.5	0.897
Glucose (mg/dL)	126.0 (76.0–380.0)	121.0 (76.0–380.0)	158.5 (80.0–371.0)	<0.001
HbA1c (%)	7.4 ± 2.0	6.9 ± 1.7	8.7 ± 2.5	<0.001
Low-density lipoprotein (mg/dL)	129.7±39.9	125.5 ± 37.9	141.9 ± 43.5	<0.001
Triglyceride (mg/dL)	154.0 (48.0–968.0)	139.0 (48.0–968.0)	198.0 (52.0–758.0)	<0.001
Triglyceride glucose index	9.1 (7.7–11.7)	9.0 (7.7–11.1)	9.8 (8.0–11.7)	<0.001
Echocardiographic variables				
Left atrial diameter (mm)	38.5 ± 4.1	37.4 ± 3.5	41.6 ± 4.2	<0.001
Left ventricular ejection fraction (%)	52.4 ± 9.2	53.3 ± 8.9	49.7 ± 9.7	0.001
Mild or moderate mitral regurgitation, n(%)	362 (87.0)	266 (85.8)	96 (90.6)	0.157
Number of distal anastomotic vessels				
1 vessel, n(%)	41 (9.9%)	34 (11.0%)	7 (6.6%)	0.001
2 vessels, n(%)	114 (27.4%)	99 (31.9%)	15 (14.2%)	<0.001
3 vessels, n(%)	261 (62.7%)	177 (57.1%)	84 (79.2%)	<0.001
Postoperative data				
Mechanical ventilation time (hours)	8.0 (2.0–46.0)	7.0 (3.5–46.0)	9.0 (2.0–39.0)	<0.001
Postoperative ICU stay (days)	3 (1–29)	3 (1–12)	4 (1–29)	<0.001
Postoperative hospital stay (days)	7 (4–104)	7 (4–22)	9 (5–104)	<0.001

Abbreviations: ACS; acute coronary syndrome, CABG; coronary artery bypass grafting, eGFR; estimated glomerular filtration rate, HbA1c; glycated hemoglobin A1c, ICU; intensive care unit, POAF; postoperative atrial fibrillation.

ejection fraction (EF) values (49.7 ± 9.7 vs. 53.3 ± 8.9 %, P=0.001). However, no notable correlations were encountered between POAF and the presence of mild or moderate mitral regurgitation (P=0.057). Compared to patients without POAF, those with POAF experienced prolonged durations of mechanical ventilation [9.0 (2.0–39.0) vs. 7.0 (3.5–46.0) hours, P<0.001] and postoperative periods in the intensive care unit [4 (1–29) vs. 3 (1–12) day, P<0.001] (Table 1).

The relationship between the TyG index and AF in individuals

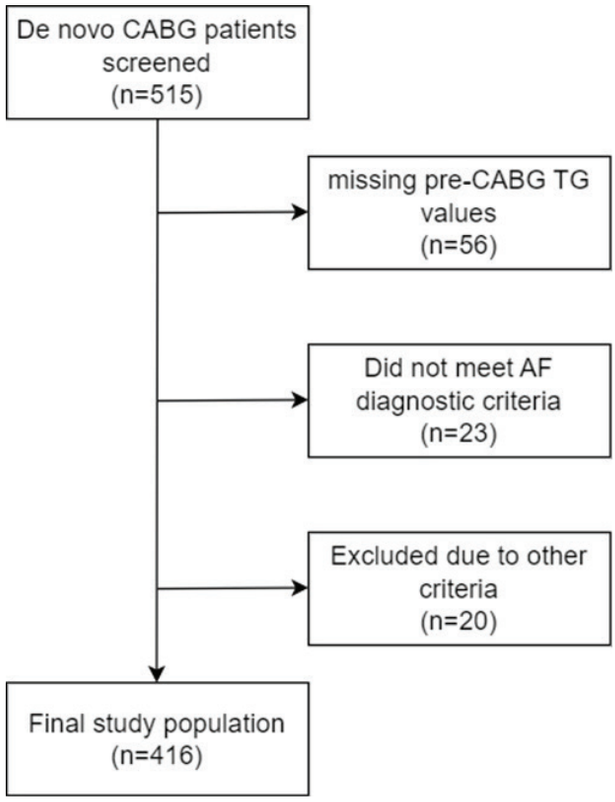

Figure 1. Flow chart
Abbreviations: AF; atrial fibrillation, CABG; coronary artery bypass grafting, TG; triglycerides

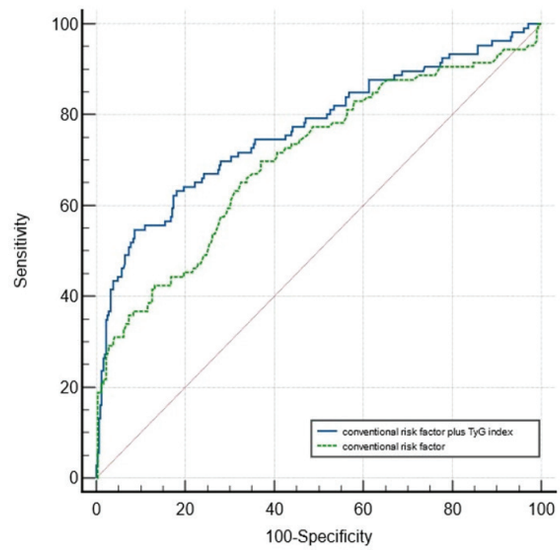

Figure 2. ROC curves of the conventional risk factor model and the conventional risk factor plus TyG index model. The conventional risk factor model includes age and left atrial diameter

with and without diabetes has yielded varied findings in previous studies [8-10]. In light of this, we conducted an analysis focusing on the TyG index and its association with AF, considering the patients' diabetic status. For non-diabetic patients, significantly elevated TyG index values were observed who developed POAF compared to those without POAF [9.5 (8.0-10.4) vs. 8.8 (7.7-9.9), P<0.001]. Additionally, a similar difference in TyG index was observed among diabetic patients who developed POAF compared to those without POAF [10.4 (8.2-11.7) vs. 9.3 (8.3-11.1), P=0.003].

The results of the univariate analysis demonstrated significant associations between POAF and various preoperative variables, including age, hyperlipidemia, diabetes mellitus, hypertension, LVEF, left atrial diameter, mechanical ventilation time, BMI, and TyG index. However, male sex and mild or moderate mitral regurgitation did not show correlations with POAF. The multivariate analysis revealed that age (odds ratio [OR]: 1.047, P=0.025), left atrial diameter (OR: 1.373, P<0.001), and TyG index (OR: 6.824, P<0.001) independently contributed to the risk of POAF, as indicated in Table 2.

The TyG index showed promise as a predictor for POAF, as evidenced by its performance in the receiver operating characteristic (ROC) curve analysis. The TyG index cutoff value of 9.38 demonstrated a sensitivity of 69.8% and a specificity of 30% in identifying patients at risk of POAF. The area under the ROC curve for the TyG index was 0.767 (95% CI: 0.709–0.826, P<0.001), indicating moderate predictive power. Notably, the inclusion of the TyG index in the model, which consisted of age and left atrial diameter, significantly enhanced its predictive capacity for POAF in patients undergoing off-pump CABG (area under the ROC curve: 0.709 (0.663–0.752) vs. 0.774 (0.731–0.813), P=0.038) (Figure 2).

Discussion

To the best of our knowledge, this study is the first to establish the TyG index as a predictor for POAF in patients undergoing isolated off-pump CABG procedures. Our findings, along with the ROC curve analysis, present notable evidence endorsing the TyG index as a reliable predictive tool to identify individuals susceptible to POAF. Moreover, including the TyG index with standard risk factors significantly enhanced our predictive ability for POAF after surgery.

The prevalence of POAF in our study was 25.5%, which closely resembles the reported rate of 24.9% in patients following CABG based on the most up-to-date data [11]. After surgical revascularization, patients who experience POAF tend to have higher postoperative morbidity and mortality rates and extended stays in the intensive care unit and hospitalization [12, 13]. According to our findings, it was revealed that patients with POAF had prolonged mechanical ventilation times and hospitalization. Hence, it may be important to identify patients at high risk for POAF in patients undergoing CABG.

In the study reported by Garg et al. [14], it was stated that either fasting or post-glucose insulin levels as indicators of IR could not predict the risk of AF. Therefore, in indices such as the homeostasis model, which requires fasting insulin levels, the TyG index emerges as an IR indicator that can provide more valuable information regarding cardiovascular events, such as

AF [15-17].

The precise mechanism connecting the TyG index to POAF has not been definitively established. However, the TyG index, as an IR marker, holds significant potential in elucidating the underlying factors contributing to the development of POAF. The TyG index formula indicates that a higher TyG index can be attributed to elevated levels of triglycerides or glucose, which in turn is indicative of impaired glucose uptake and utilization, a hallmark characteristic of IR. An animal experiment showed that IR caused changes in atrial structure in rats. It has also been shown that it increases the sensitivity of cells to AF by disrupting the calcium balance within cells because of hyperglycemia [18]. Studies have indicated that irregular handling of calcium ions (Ca2+) is associated with abnormal electrical activity that triggers AF [18, 19]. Given the detrimental effects of hyperglycemia on calcium Ca2+ regulation, it can exert a considerable impact on atrial electrical and structural remodeling, hence contributing to the initiation of AF [20, 21].

Consistent with prior studies, our research demonstrates a robust association between IR and AF [3, 4]. Chen et al. [8] supported the meaningful role of the TyG index as a predictor of AF, serving as a marker for IR. They utilized the TyG index, presented compelling evidence indicating a meaningful correlation between IR and AF, and observed a higher prevalence of AF among hospitalized patients with elevated TyG index values. Notably, the TyG index maintained its independent association with AF, even after adjusting for other predisposing factors [8].

Our study revealed an association between increased TyG index levels and POAF in diabetic and non-diabetic patients. Although this connection has been established in previous research for non-diabetic patients [8, 9], the significant link between the TyG index and AF in diabetic patients remains less extensively explored. Shi et al. [22] conducted a study involving 3244 diabetic patients and found a strong linear correlation between the TyG index and AF prevalence in diabetic patients. Their findings indicated the TyG index's potential to enhance AF detection among individuals with diabetes. The primary driver of oxidative stress in diabetes is hyperglycemia, which triggers the generation of reactive oxygen species This oxidative stress is implicated in initiating cellular changes within atrial tissue, leading to disturbances in electrical activity—a pivotal factor contributing to the development of POAF [23]. In our study, the TyG index's predictive efficacy for POAF among diabetic patients might be attributed to its incorporation of high blood glucose levels, a TyG index component, and its association with heightened oxidative stress. This suggests a potential mechanistic pathway through which the TyG index could serve as a valuable prognostic marker for identifying individuals at risk of developing POAF in the context of diabetes.

In patients undergoing cardiac surgery, advanced age has been widely recognized as a primary risk factor for the development of POAF. Additionally, left atrial enlargement has shown a strong correlation with the predictive value for POAF [1, 24]. Therefore, we included age and left atrial diameter as conventional risk factors in our predictive model to assess the TyG index's ability to predict POAF. Similarly, a study conducted by Wei et al. [25] on patients who underwent septal myectomy found that the TyG index independently predicted the occurrence of POAF. However, unlike their findings, the inclusion of the TyG index in our model significantly enhanced the accuracy of our predictive model, enabling the identification of patients at risk of developing POAF.

Limitation

Our study has certain limitations that should be acknowledged. Firstly, the retrospective design restricted our ability to capture all potential factors that could influence the occurrence of POAF. Additionally, the fasting plasma triglyceride and glucose levels assessment was limited to a single measurement before surgery, preventing us from evaluating the impact of changes in the TyG index on POAF. Lastly, the generalizability of our findings to other cardiac surgical procedures, such as on-pump CABG, may be limited as our study exclusively focused on off-pump CABG patients.

Conclusion

In the patients undergoing off-pump CABG, the TyG index was a notable independent predictor for POAF, regardless of their diabetic status. However, more large-scale multicenter and prospective studies are needed to confirm its efficacy before it can be used in clinical practice.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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